

## **AMENDMENTS TO THE CLAIMS:**

The listing of claims will replace all prior versions, and listings of claims in the application:

## **LISTING OF CLAIMS:**

### **Claims 1 to 18 (canceled)**

**Claim 19 (new)** An axon sprouting stimulation kit comprising

- a first container means comprising a first fibrin matrix forming element,
- a second container means comprising a second fibrin matrix forming element,
- a mixing means for intermingling said first and second fibrin matrix forming elements into a therapeutically acceptable fibrin matrix, and;
- a delivery means,

wherein at least one of said first and second container means further comprises a matrix-releasable therapeutically active agent selected from the group consisting of C3, Y-27632, Y-30141 for facilitating axon sprouting at a nerve lesion site.

**Claim 20 (new)** The axon sprouting stimulation kit of claim 19, wherein C3 is selected from the group consisting of ADP-ribosyl transferase C3 derived from Clostridium botulinum, a C3 polypeptide having an insertion in one or more amino acids and retaining ADP-ribosylation activity, a C3 polypeptide having a substitution in one or more amino acids and retaining ADP-ribosylation activity, a C3 fragment retaining ADP-ribosylation activity and a recombinant C3 retaining ADP-ribosylation activity.

**Claim 21 (new)** The axon sprouting stimulation kit of claim 19, wherein one of said first or second fibrin matrix forming element is fibrinogen and the other of said first and second fibrin matrix forming element is a component for cleaving fibrinogen.

**Claim 22 (new)** The axon sprouting stimulation kit of claim 19, wherein one of said first or second fibrin matrix forming element is fibrinogen and the other of said first or second fibrin matrix forming element is thrombin and wherein at least one of said first and second container means comprises calcium chloride.

**Claim 23 (new)** The axon sprouting stimulation kit of claim 19, further comprising, in one of said container means, a factor for catalyzing the cross-linkage of fibrin.

**Claim 24 (new)** The axon sprouting stimulation kit of claim 23, wherein said factor is selected from the group consisting of Factor XIII and Factor XIIIa.

**Claim 25 (new)** The axon sprouting stimulation kit of claim 19, further comprising a protease inhibitor.

**Claim 26 (new)** The axon sprouting stimulation kit of claim 19, further comprising fibronectin in one of said container means.

**Claim 27 (new)** The axon sprouting stimulation kit of claim 19, further comprising, in one of said container means, an inhibitor selected from the group consisting of a plasminogen activator inhibitor and a plasmin inhibitor.

**Claim 28 (new)** The axon sprouting stimulation kit of claim 27, wherein said plasmin inhibitor is aprotinin.

**Claim 29 (new)** The axon sprouting stimulation kit of claim 19, further comprising a polysaccharide in one of said container means.

**Claim 30 (new)** The axon sprouting stimulation kit of claim 29, further comprising an inhibitor of polysaccharide degradation in one of said container means.

**Claim 31 (new)** The axon sprouting stimulation kit of claim 29, wherein said polysaccharide is hyaluronic acid.

**Claim 32 (new)** The axon sprouting stimulation kit of claim 31, further comprising an inhibitor of hyaluronic acid degradation in one of said container means.

**Claim 33 (new)** The axon sprouting stimulation kit of claim 32, wherein the inhibitor of hyaluronic acid degradation is a hyaluronidase inhibitor.

**Claim 34 (new)** An axon sprouting stimulation kit comprising

- a first container means comprising a first fibrin matrix forming element,
- a second container means comprising a second fibrin matrix forming element,
- a third container means comprising a therapeutically active agent selected from the group consisting of C3, Y-27632 and Y-30141 for facilitating axon sprouting at

said lesion site,

- a mixing means for intermingling the content of said first, second and third container to form a therapeutically acceptable fibrin matrix containing a therapeutically active agent, and;

- a delivery means,

wherein said therapeutically active agent is releasable from said therapeutically acceptable fibrin matrix into an adjacent external environment.

**Claim 35 (new)** The axon sprouting stimulation kit of claim 34, wherein C3 is selected from the group consisting of ADP-ribosyl transferase C3 derived from Clostridium botulinum, a C3 polypeptide having an insertion in one or more amino acids and retaining ADP-ribosylation activity, a C3 polypeptide having a substitution in one or more amino acids and retaining ADP-ribosylation activity, a C3 fragment retaining ADP-ribosylation activity and a recombinant C3 retaining ADP-ribosylation activity.

**Claim 36 (new)** The axon sprouting stimulation kit of claim 34, wherein one of said first or second fibrin matrix forming element is fibrinogen and the other of said first or second fibrin matrix forming element is a component for cleaving fibrinogen.

**Claim 37 (new)** The axon sprouting stimulation kit of claim 34, wherein one of said first or second fibrin matrix forming element is fibrinogen and the other of said first or second fibrin matrix forming element is thrombin and wherein at least one of said first and second container means comprises calcium chloride.

**Claim 38 (new)** A biocompatible composition for facilitating axon sprouting, said composition comprising: (i) a therapeutically active agent selected from the group consisting of C3, Y-30141 and Y-27632 for facilitating axon sprouting, and (ii) a fibrin matrix forming element.

**Claim 39 (new)** The biocompatible composition of claim 38, wherein said fibrin matrix forming element is selected from the group consisting of fibrinogen and a component for cleaving fibrinogen.

**Claim 40 (new)** The biocompatible composition of claim 39, further comprising calcium chloride and wherein said component is thrombin.

**Claim 41 (new)** The biocompatible composition of claim 38, wherein C3 is selected from

the group consisting of ADP-ribosyl transferase C3 derived from *Clostridium botulinum*, a C3 polypeptide having an insertion in one or more amino acids and retaining ADP-ribosylation activity, a C3 polypeptide having a substitution in one or more amino acids and retaining ADP-ribosylation activity, a C3 fragment retaining ADP-ribosylation activity and a recombinant C3 retaining ADP-ribosylation activity.

**Claim 42 (New)** A kit for forming, in vivo at a nerve lesion site, a therapeutically acceptable fibrin matrix containing a releasable therapeutic Rho antagonist agent which elicits axon sprouting,

the therapeutic Rho antagonist agent selected from the group consisting of  
Y-27632,  
Y-30141,  
C3 protein from *Clostridium botulinum*,  
recombinant C3 proteins that retain ADP-ribosylation activity, and  
truncation protein fragments of C3 retaining ADP-ribosylation activity to  
inactivate Rho GTPase, wherein the truncation of one or more amino acids may  
originate from the amino terminus of the C3 protein, from the carboxy terminus of  
the C3 protein, or from the interior of the C3 protein,

the kit comprising:  
a first solution comprising fibrinogen in a first container,  
a second solution comprising thrombin and calcium chloride in a second  
container,  
wherein at least one of said first solution and said second solution further comprises  
said therapeutic Rho antagonist agent,

a means for mixing said first solution and said second solution to form an  
activated solution of polymerizable fibrin containing said therapeutic Rho antagonist  
agent which elicits axon sprouting; and

a means for application of said activated solution to said lesion site,  
wherein polymerization of said polymerizable fibrin occurs at the lesion site  
within about 10 seconds after said application, and

wherein said therapeutic Rho antagonist agent is releasable from said  
matrix into the adjacent external environment.

**Claim 43 (New)** The kit of claim 42, wherein the first container further comprises a  
component selected from the group consisting of Factor XIII and aprotinin.

**Claim 44 (New)** The kit of claim 42, wherein the first solution comprises fibrinogen

at 75 mg/ml, glycine buffer comprising 2 mg/ml of sodium chloride (NaCl) and 4 mg/ml of trisodium citrate and 15 mg/ml of glycine, and aprotinin at 3000 KIU/ml.

**Claim 45 (New)** The kit of claim 42, wherein the second solution comprises 500 IU/ml thrombin, 2.4 mg/ml glycine, 8 mg/ml sodium chloride, and 40  $\mu$ mol/ml calcium chloride.

**Claim 46 (New)** The kit of claim 42, wherein the application is by means of a syringe and needle.

**Claim 47 (New)** The kit of claim 42, wherein the means for mixing is a syringe selected from the group consisting of a single syringe, a syringe having a mixing compartment, two syringes attached by a three-way stopcock, and two syringes having a common plunger.

**Claim 48 (New)** The kit of claim 42, wherein the therapeutic Rho antagonist agent is present as a substantially uniform dispersion in the activated solution.

**Claim 49 (New)** The kit of claim 42, wherein the therapeutic Rho antagonist agent is a C3 protein present as a dose of about 3 grams per 60 kilogram person.

**Claim 50 (New)** The kit of claim 42, wherein the therapeutic Rho antagonist agent is a C3 protein present at a concentration of 25 to 50 micrograms per milliliter.

**Claim 51 (New)** The kit of claim 42, wherein the therapeutic Rho antagonist agent is a C3 protein present at a concentration of 1/3 milligrams per milliliter.

**Claim 52 (New)** The kit of claim 42, wherein the lesion site is in an injured spinal cord.